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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/315,298	05/20/1999	CHING-LEOU TENG	ISIS-3510	6350

34138 7590 09/26/2005

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/315,298	TENG ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 9-16-2005.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,4-7,13,19,20,80,84,85,91,95 and 97 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,4-7,13,19,20,80,84,85,91,95 and 97 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1, 4-7, 19-20, 80, 84-85, 91, 95, and 97 are presently pending.

Response to Arguments

Claim Rejections - 35 USC § 102

3. The rejection of Claims 1, 5, 13, 91 and 95 under 35 U.S.C. 102(e or b) as being anticipated by Yiv (US 5,707,648 or WO 95/14037) is withdrawn in response to Applicant's arguments filed 9-16-05.

Claim Rejections - 35 USC § 103

4. Claims 1, 4-7, 13, 19-20, 80, 84-85, 91, and 95 remain rejected and *new claim 97 is rejected* under 35 U.S.C. 103(a) as being unpatentable over Kawai et al. in view of Yiv (US 5707648 A; or WO 95/14037), Bennett et al. (US Patent No. 5,514,788) and Nielsen et al., for the reasons of record set forth in the prior Office Action.

5. Applicant's arguments filed 9-16-05 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that each of the references cited by the examiner provide only broad teachings regarding formulations. According to Applicants there is no motivation to select the specific formulations claimed in the instant invention as required for a proper obviousness type rejection. Moreover, Applicants argue that the small number of species claimed would not be obvious in view of the teachings of large genuses of penetration enhancers in the prior art, and furthermore according to Applicants, the enhanced bioavailability of oligonucleotides

that is produced by the formulations of the instant invention is not obvious in view of the references cited.

6. Contrary to Applicant's assertions, regarding motivation to combine, the prior art clearly teaches that microemulsion preparations comprising a fatty acid are useful for the delivery of nucleic acid molecules into cells, see page 34, 2nd col. of the translation of Kawai et al. Additionally, in regards to motivation for using the bile salts CDCA and UDCA, although Yiv discloses multiple penetration enhancers, it is clear that each enhancer is disclosed in this reference as functionally equivalent alternative compounds, wherein each bile salt having the ability to enhance the mucosal absorption of a drug, and wherein the drug of Yiv includes an antisense compound (see col. 12, lines 20-31 and 56-67 of Yiv). In regards to the enhanced bioavailability observed by Applicants, as described on page 7, paragraph 3 of the response filed 9-16-2005, specifically in Example 11 and Table 18 of the specification as filed, Applicant's enhanced bioavailability observed using the emulsion formulations described in Example 11 and Table 18 are limited to a combination of specific components, namely Labrasol, Captex, and Grill 3, the instant claims are not limited to the particular three component emulsion formulations described in the specification as filed to possess enhanced bioavailability. The instant claims are generically drawn to a composition comprising at least one oligonucleotide in an emulsion, and a bile salt (CDCA or UDCA) and a fatty acid. Applicants have not provided any evidence that the properties associated with using the specific emulsions used in the formulations described in Table 18 would be representative for the full scope of the compositions instantly claimed to

comprise generically an emulsion. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

New claim 97 is also considered to be obvious over Kawai et al. in view of Yiv (US 5707648 A; or WO 95/14037), Bennett et al. (US Patent No. 5,514,788) and Nielsen et al., since the compositions of Kawai et al. are disclosed as comprising a transducing-gene DNA and a fat emulsion base of at least one kind chosen from a vegetable oil, triglyceride of the medium chain triglyceride of 8-12 carbon atoms (such as capric, lauric and caprylic acid, see page 16, paragraph [0013]), fatty acids of 6-18 carbon atoms. Although capric acid is disclosed as one of several fatty acids, it is clear that each fatty acid is disclosed as being functionally equivalent obvious alternative fatty acids that are useful in the compositions of Kawai et al.

As stated previously, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the teachings of Kawai et al., Yiv, Bennett et al. and Nielsen et al. to make the claimed invention. Absent any evidence of unexpected results associated with the compositions as claimed, it would have been obvious to one of ordinary skill in the art at the time of filing to modify the compositions of Kawai et al., which comprise a microemulsion formulation and a fatty acid, to further comprise bile salts, or to comprise the oligonucleotides disclosed in Bennett et al. and Nielsen et al. One of ordinary skill in the art would have been motivated to make these modification since the compositions of Kawai et al. are intended to provide carriers suitable for intracellular delivery of DNA associated with cancer suppression genes, and

DNA relevant to viral illness, and the antisense oligonucleotides of Bennett et al. and Nielsen et al. are disclosed as being useful for inhibiting the expression of genes associated with cancer (see col. 5, lines 45-47 of Bennett et al.) and viral infection (see abstract of Nielsen et al.), respectively. Moreover, one of ordinary skill in the art would have been motivated to modify the compositions of Kawai et al. with the bile salts of Yiv for the expressed benefits of the presence of bile salts in pharmaceutical compositions according to Yiv, specifically wherein the bile salts function to improve mucosal absorption of biologically active materials.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford
Examiner
Art Unit 1633

JLE